Depression in adults: psychological treatments and care pathways

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ABSTRACT

INTRODUCTION: Depression may affect up to 10% of the population, with symptoms recurring in half of affected people. In mild to moderate depression, there is no reliable evidence that any one treatment is superior in improving symptoms of depression, but the strength of evidence supporting different treatments varies. METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical questions: What are the effects of psychological treatments, and of interventions to reduce relapse rates, in mild to moderate or severe depression? What are the effects of psychological interventions to improve delivery of treatments in mild to moderate or severe depression? We searched: Medline, Embase, The Cochrane Library and other important databases up to April 2006 (BMJ Clinical Evidence reviews are updated periodically, please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). RESULTS: We found 55 systematic reviews, RCTs, or observational studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions. CONCLUSIONS: In this systematic review we present information relating to the effectiveness and safety of the following interventions: befriending, care pathways, cognitive therapy, combining antidepressant drugs and psychological treatments, interpersonal psychotherapy, non-directive counselling, problem-solving therapy, relapse prevention programme.

QUESTIONS

INTERVENTIONS

Key points

- Depression may affect up to 10% of the population, with symptoms recurring in half of affected people.
- In mild to moderate depression, there is no reliable evidence that any one treatment is superior in improving symptoms of depression, but the strength of evidence supporting different treatments varies.

- Cognitive behavioural therapy and interpersonal psychotherapy reduce symptoms of mild to moderate depression, although many of the trials have been small.

  Combining psychological treatment with antidepressant drugs may be more effective than either treatment alone.

  Non-directive counselling may also be effective, but we don't know whether problem-solving therapy or befriending are beneficial.

  Care pathways may improve the effectiveness of treatment for depression.

- We don't know whether cognitive behavioural therapy or relapse prevention programmes are beneficial in reducing the risk of relapse after recovery.

DEFINITION

Depressive disorders are characterised by persistent low mood, loss of interest and enjoyment, and reduced energy. They often impair day to day functioning. Most of the RCTs assessed in this review classify depression using the *Diagnostic and Statistical Manual of Mental Disorders IV* (DSM)-IV [1] or the *International Classification of Mental and Behavioural Disorders 10* (ICD)-10. [2] DSM-IV divides depression into major depressive disorder or dysthymic disorder. **Major depressive disorder** is characterised by one or more major depressive episodes (i.e. at least 2 weeks of depressed mood or loss of interest accompanied by at least 4 additional symptoms of depression). **Dysthymic disorder** is characterised by at least 2 years of depressed mood for more days than not, accompanied by additional symptoms that do not reach the criteria for major depressive disorder. [1] ICD-10 divides depression into mild to moderate or severe depressive episodes. [2] Mild to moderate depression is characterised by depressive symptoms and some functional impairment. Severe depression is characterised by additional agitation or psychomotor retardation with marked somatic symptoms. [2] **Treatment-resistant depression** is defined as an absence of clinical response to treatment with a tricyclic antidepressant at a minimum dose of 150 mg daily of imipramine (or equivalent drug) for 4–6 weeks. [3] In this review, we use both DSM-IV and ICD-10 classifications, but treatments are considered to have been assessed in severe depression if the RCT included inpatients. **Older adults:** Older adults are generally defined as people aged 65 years or older. However, some of the RCTs of older people in this review included people aged 55 years or over. The presentation of depression in older adults may be atypical: low mood may be masked, and anxiety or memory impairment may be the principal presenting symptoms. Dementia should be considered in the differential diagnosis of depression in older adults. [4] **Treating depressive disorders in adults:** Depressive disorders are generally treated with a range of drug, physical, and psychological treatments. For coverage of drug and other physical treatments, see review on depression in adults: drug and physical treatments. Combined drug and psychological treatment and comparisons of psychological versus drug treatment are covered in this review. **Population:** This review does not cover intervention in women with postnatal depression (see review on postnatal depression), seasonal affective disorder, or depression because of a physical illness such as stroke or substance abuse.

INCIDENCE/ PREVALENCE

Depressive disorders are common, with a prevalence of major depression between 5% and 10% of people seen in primary care settings. [5] Two to three times as many people may have depressive symptoms but do not meet DSM-IV criteria for major depression. Women are affected twice as often as men. Depressive disorders are the fourth most important cause of disability worldwide, and are expected to become the second most important cause by 2020. [6] [7] **Older adults:** Between 10% and 15% of older people have depressive symptoms, although major depression is less common among older adults. [8]

AETIOLOGY/ RISK FACTORS

The causes of depression are uncertain, but are thought to include both childhood events and current psychosocial adversity. Recent studies suggest that genetic factors may also be important, indicating that several chromosomal regions may be involved. However, phenotypes do not seem to exhibit classic Mendelian inheritance. Psychiatric research has also focused on the role that psychosocial factors, such as social context and personality dimensions, have in depression. Many theories emphasise the importance of temperament (differences in the adaptive systems), which can increase vulnerability to mood disturbances. Impairment in social relationships, gender, socioeconomic status, and dysfunctional cognition may also be involved. It seems that integrative models, which take into account the interaction of biological and social variables, offer the most reliable way to approach the complex causes of depression.

PROGNOSIS

About half of people suffering a first episode of major depressive disorder experience further symptoms in the subsequent 10 years. [9] **Older adults:** One systematic review (search date 1996, 12 prospective cohort studies, 1268 people, mean age 60 years) found that the prognosis may be especially poor in elderly people with a chronic or relapsing course of depression. [10] Another systematic review (search date 1999, 23 prospective cohort studies in people aged 65 years or over, including 5 identified by the first review) found that depression in older people was associated with increased mortality (15 studies; pooled OR 1.73, 95% CI 1.53 to 1.95). [11]

AIMS OF INTERVENTION To improve mood, social and occupational functioning, and quality of life; to reduce morbidity and mortality; to prevent recurrence of depressive disorder; and to minimise adverse effects of treatment.

OUTCOMES Depressive symptoms rated by the depressed person and clinician; social functioning; occupational functioning; quality of life; admission to hospital; rates of self harm; relapse of depressive symptoms; rates of adverse events. RCTs often use continuous scales to measure depressive symptoms (such as the Hamilton Depression Rating Scale [HAM-D], the Clinical Global Impression Scale [CGI], the Beck Depression Inventory [BDI], and the depression scale from the Hopkins Symptom Checklist). A reduction in score of 50% or more on these scales or a CGI score of 1 (very much improved) or 2 (much improved) is generally considered a clinically important response to treatment. Many RCTs express results in terms of effect size. **Older adults:** The HAM-D is not ideal for older people because it includes several somatic items that may be positive in older people who are not depressed. It has been the most widely used scale, although specific scales for elderly people (such as the Geriatric Depression Scale [GDS]) avoid somatic items.

METHODS *BMJ Clinical Evidence* search and appraisal April 2006. The following databases were used to identify studies for this review: Medline 1966 to April 2006, Embase 1980 to April 2006, Psychinfo 1980 to April 2006, and The Cochrane Library and Cochrane Central Register of Controlled Clinical Trials Issue 1, 2006. Additional searches were carried out using these websites: NHS Centre for Reviews and Dissemination (CRD) — for Database of Abstracts of Reviews of Effects (DARE) and Health Technology Assessment (HTA), Turning Research into Practice (TRIP), and National Institute for Health and Clinical Excellence (NICE). Abstracts of the studies retrieved were assessed independently by two information specialists using predetermined criteria to evaluate relevant studies. Study design criteria for inclusion in this review were: published systematic reviews and RCTs in any language, at least single blinded, and containing more than 20 individuals of whom more than 80% were followed up. There was no minimum length of follow-up required to include studies. We excluded all studies described as "open", "open label", or not blinded unless blinding was impossible. We also did a search for cohort studies on specific harms of named interventions. In addition, we use a regular surveillance protocol to capture harms alerts from organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA), which are added to the review as required. In this review, studies are included under the heading **older adults** if they specifically included people aged over 55 years. We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 20).

QUESTION What are the effects of psychological treatments in mild to moderate or severe depression?

OPTION COGNITIVE THERAPY FOR INITIAL TREATMENT

Symptom severity

Compared with placebo/waiting list control/usual care Cognitive therapy may be more effective at improving symptoms in people with depression or dysthymia (low-quality evidence).

Compared with no treatment (older adults) Cognitive and behavioural therapy are more effective at improving symptoms (measured as Hamilton Depression Rating Scale [HAM-D] score) in older adults in an outpatient or community setting (moderate-quality evidence).

Treatment success

Compared with control (usual care, usual care plus pill placebo, or supportive therapy) Psychological therapies (mainly interpersonal psychotherapy and cognitive therapy) may be more effective at increasing the proportion of people in remission at 10–34 weeks compared with control (low-quality evidence).

Compared with other psychological therapies (interpersonal therapy, combined interpersonal therapy, brief psychodynamic therapy, or supportive therapy) We don't know whether cognitive therapy is more effective at increasing the proportion of people who recover or are at remission (very low-quality evidence).

For GRADE evaluation of interventions for depression in adults: psychological treatments and care pathways, see table, p 20 .

Benefits: We found seven systematic reviews (see table 1, p 17). [12] [13] [14] [15] [16] [17] [18] The reviews compared different populations and different combinations of psychotherapies in the experimental and comparison treatments. We also found one subsequent RCT. [19] The first systematic review compared cognitive therapy with any other intervention. [12] It found that cognitive therapy was better than a combined group of placebo and waiting list controls, drug treatment, and "other therapies", but not behavioural therapy (search date not reported, 48 RCTs, 2765 adults with major depression or dysthymia, none of whom were psychotic or had bipolar disorder, most were outpa-

tients; see table 1, p 17). This review has been criticised for grouping together dissimilar treatments as comparisons — for example, grouping placebo and waiting list controls. "Other therapies" incorporated, for example, supportive and non-directive psychotherapies, relaxation therapy, and interpersonal psychotherapy. [20] A subsequent re-analysis of these studies separated "other therapies" into "bona fide" (intended to have a therapeutic effect) and "non-bona fide" (not intended to have a therapeutic effect) treatments for depression. The review found that cognitive therapy was as effective in treating depression as "bona fide" non-cognitive therapy and behavioural treatments, but more effective than non-bona fide treatments. [21] The second review (search date 2000, 6 RCTs, 883 outpatients with mild to moderate depression) compared three treatments: psychotherapy (primarily cognitive therapy and interpersonal therapy); antidepressants; and placebo. [13] The review found that psychotherapy and medication significantly increased remission rates compared with control (proportion remitting: 46.3% with psychotherapy *v* 46.4% with medication [tricyclic antidepressants and phenelzine] *v* 24.4% with control; P < 0.0001). [13] The third review compared any psychotherapy with various different psychological treatments (including cognitive behavioural therapy [CBT]). [14] The review (search date 1999, 12 RCTs, 654 adults aged 16–65 years with depression) found that CBT significantly improved recovery rates compared with treatment as usual (recovery: OR 3.4, 95% CI 2 to 6). [14] The review found no significant difference between CBT and interpersonal therapy in recovery rates (2 RCTs, 275 people; recovery: OR 1.08, 95% CI 0.70 to 1.70). [14] The review also found that CBT significantly improved recovery rates compared with supportive therapy (10 RCTs, 409 people; recovery: OR 3.45, 95% CI 1.30 to 9.20). [14] Cognitive therapy also increased recovery compared with combined group of interpersonal therapy, brief psychodynamic therapy, or supportive therapy (see table 1, p 17). The review concluded that brief psychological therapies are beneficial in the treatment of people with depression managed outside hospital settings. The fourth review (search date not reported) examined the effectiveness of treating depressive disorder in primary care. [15] It found two cognitive therapy studies, one of which was included in a previous review. The second RCT (464 people with depression or mixed anxiety and depression) compared CBT with non-directive counselling in two separately randomised arms. The first arm, which compared CBT versus non-directive counselling versus usual care, found no significant difference between treatment arms and usual care, but did not perform a between-treatment-group analysis. The second arm compared CBT versus non-directive counselling and found no significant difference between treatments in symptoms of depression after 12 months (Beck Depression Inventory [BDI] score: 12.5 with CBT *v* 12.8 with non-directive counselling; reported as not significant; no further details reported). [22] Overall, the review found that all psychological therapies improved depressive symptoms compared with usual care. However, it did not provide separate results for cognitive therapy. The fifth review compared CBT with short-term psychodynamic therapy (including interpersonal therapy). [16] The review did not perform a meta-analysis, but overall found no significant difference between CBT and psychodynamic therapy (search date 1998, 6 studies, 497 outpatients with depression). [16] The sixth systematic review (search date 2002, 11 RCTs, 348 adults randomised to cognitive therapy) carried out a meta-analysis of RCTs that compared cognitive therapy versus waiting list, pill placebo, or attention/psychological controls (see table 1, p 17). [17] The review found an effect size of 0.77 for cognitive therapy in improving the symptoms of depression, but the result was not significant (95% CI 0.44 to 1.10). However, the review reported that there was heterogeneity between the studies, and so the results should be interpreted with caution. The authors noted that the magnitude of the effect size was dependent on the type of control treatment and the baseline severity of the patients. The seventh systematic review (search date 2002) compared cognitive therapy versus interpersonal therapy. [18] The review found cognitive therapy to be significantly less effective than interpersonal therapy in improving the symptoms of depression (see table 1, p 17). However, the review found no significant difference in remission rates between the two treatments. The subsequent RCT [19] (240 people aged 18–70 years with a *Statistical Manual of Mental Disorders IV* (DSM)-IV diagnosis of major depressive disorder and a Hamilton Depression Score [HAM-D] > 20) compared cognitive therapy (60 people) versus paroxetine (120 people) and pill placebo (60 people). The RCT defined a response as a Hamilton Depression Score of 12 or less. The RCT found that both cognitive therapy and paroxetine significantly improved symptoms of depression compared with pill placebo after 8 weeks (response rate with cognitive therapy: 43% with cognitive therapy *v* 25% with pill placebo; P = 0.04; response rate with paroxetine: 50% with paroxetine *v* 25% with pill placebo; absolute numbers not reported; P = 0.001). However, the RCT found no significant difference in response rate between cognitive therapy and paroxetine (P = 0.40). After 16 weeks, 58% of people in both the cognitive therapy and paroxetine groups met the response criteria. The RCT found no significant difference in response rate between the two treatments (P = 0.92). The authors noted that the experience of the cognitive therapist could influence outcomes, with more experienced cognitive therapists producing improved outcomes.

Older adults:

We found one systematic review of pharmacological and psychological treatments (search date 1995, 14 RCTs of psychological therapies, 587 people aged > 55 years in an outpatient or commu-

nity setting). [23] It found four RCTs that compared cognitive or behavioural therapy versus no treatment. It found that cognitive and behavioural therapy significantly improved symptoms compared with no treatment (mean difference in the Hamilton Depression Rating Scale [HAM-D] score –7.3, 95% CI –10.1 to –4.4, see table 1, p 17). [23]

Harms:

Five of the reviews gave no information on adverse effects. [13] [15] [16] [17] [18] The second review found that significantly more people withdrew from control conditions than from treatment with either medication or psychotherapy (22% with psychotherapy *v* 37% with medication *v* 55% with control; reported as significant). [13] The fourth review stated that reporting of adverse effects in the RCTs it identified was poor, and that consequently it could not draw any conclusions about adverse effects of psychological therapies. [14] The subsequent RCT reported that, after 8 weeks, four people in the cognitive therapy group withdrew because of dissatisfaction with the treatment. Withdrawals caused by adverse effects occurred in only the paroxetine (8/120 [7%]) and pill placebo (2/60 [3%]) groups. [19]

Older adults:
The review gave no information on adverse effects. [23]

Comment:

Large RCTs are needed in more representative people in a range of clinical settings, including primary care. Because of varying exclusion criteria, the generalisability of the studies is questionable (see table 1, p 17). Other factors to be considered when psychological treatments are compared with drug treatment include whether serum concentrations of drugs reach therapeutic concentrations, whether changes in medication are allowed (reflecting standard clinical practice), and whether studies reflect the natural course of depressive disorders. It is difficult to conduct studies of psychological treatments for severe depression because of the ethics surrounding withholding a proven treatment (prescription antidepressant drugs) in a group of people at risk of self harm or neglect. [24]

OPTION INTERPERSONAL PSYCHOTHERAPY FOR INITIAL TREATMENT

Treatment success
Compared with usual care/no treatment Interpersonal psychotherapy for initial treatment is more effective at increasing the proportion of people who recover from depression (moderate-quality evidence).

Compared with no treatment (in older adults) We don't know whether interpersonal psychotherapy is more effective as a treatment for depression (very low-quality evidence).

Compared with cognitive behaviour therapy/antidepressants Interpersonal psychotherapy and cognitive therapy, or interpersonal psychotherapy plus antidepressants and antidepressants alone seem to be equally effective at reducing remission rates (moderate-quality evidence).

Symptom severity
Compared with placebo/cognitive behaviour therapy Interpersonal psychotherapy is more effective at improving symptoms of depression (high-quality evidence).

For GRADE evaluation of interventions for depression in adults: psychological treatments and care pathways, see table, p 20 .

Benefits:

We found three systematic reviews [13] [14] [15] and one subsequent RCT [25] which compared interpersonal therapy versus usual care. We found one review that compared interpersonal therapy versus antidepressant medication or cognitive therapy. [18] It also compared interpersonal therapy plus medication versus medication alone. Two reviews did not report outcomes for interpersonal therapy alone. [13] [15] One review and the subsequent RCT found that interpersonal psychotherapy improved symptoms of depression compared with usual care (see table 1, p 17). [14] [25] The fourth review found that interpersonal therapy was more effective than cognitive therapy and placebo for depressive disorders. It also found interpersonal therapy to be as effective as medication. Efficacy of interpersonal therapy did not increase when combined with medication (see table 1, p 17). [18] RCTs found insufficient evidence to assess the relative efficacy of drug and non-drug treatment in severe depression (see comment below). The subsequent RCT found that group interpersonal psychotherapy significantly reduced numbers with depression after treatment compared with no treatment (224 people with depression in Uganda; numbers with depression after treatment: 7% with interpersonal psychotherapy *v* 55% with no treatment; reported as significant). [25]

In older adults:
We found one systematic review that compared psychodynamic or interpersonal psychotherapy versus no treatment in older adults. It found no significant difference between treatments (3 RCTs, reported as not significant, no further details reported). [23]

Harms: Three of the reviews gave no information on adverse effects. [13] [15] [18] One review stated that reporting of adverse effects in the RCTs it identified was poor, and that consequently it could not draw any conclusions about adverse effects of psychological therapies. [14]

Older adults:
The review gave no information on adverse effects. [23]

Comment: See comment on cognitive therapy, p 9 . The language of psychotherapy research is confusing. Nowhere is this better illustrated than with interpersonal therapy, which in some reviews is included as a psychodynamic intervention, and in others as a form of cognitive behavioural therapy. Consumers of studies and reviews should note the potential for confusion.

OPTION COMBINING PSYCHOLOGICAL TREATMENTS AND ANTIDEPRESSANT DRUGS FOR INITIAL TREATMENT

Symptom severity
Compared with drug treatment or interpersonal psychotherapy alone Combination of pharmacotherapy and psychotherapy is more effective at improving depressive symptoms at 12 weeks (moderate-quality evidence).

Compared with drug treatment or cognitive therapy alone (in older adults) Desipramine plus cognitive behavioural therapy may be more effective at improving symptoms at 16–20 weeks in older adults with major depressive disorders (low-quality evidence).

Treatment success
Compared with drug treatment or psychotherapies alone Combination of antidepressants and psychological treatments, and either treatment alone seem to be equally effective at increasing the proportion of people who respond to treatment (improvement in Montgomery–Asberg Depression Rating Scale [MADRS] scores) at 18 months, and achieve remission (moderate-quality evidence).

Note
There is emerging consensus that medication is better for rapid symptom relief, and psychotherapy at preventing relapse.

For GRADE evaluation of interventions for depression in adults: psychological treatments and care pathways, see table, p 20 .

Benefits: We found two systematic reviews [26] [27] and two subsequent RCTs (3 publications), [28] [29] [30] which examined the effects of combined pharmacotherapy and psychological treatment for depression. The first review found that combination treatment significantly improved depressive symptoms compared with drug treatment alone (search date 2002, 16 RCTs, 1842 people with depression; improvement in depression: OR 1.86, 95% CI 1.38 to 2.52). [26] Subgroup analysis found a greater effect in studies which were longer than 12 weeks compared with those with shorter treatment times (improvement in depression: OR 2.20, 95% CI 1.22 to 4.03). [26] There was also a significant reduction in withdrawals (further details about reasons for withdrawal not reported) from treatment with combination therapy compared with drug treatment alone. The second systematic review found evidence for a small but significant effect of combination treatment compared with medical treatment alone (search date not reported, 17 studies, number of people not reported; effect size: Cohen's d = 0.34 with Beck Depression Inventory [BDI] and 0.18 with HDRS; further details not reported). [27] The first subsequent RCT found no significant difference between sertraline alone and sertraline plus interpersonal therapy in the proportion of people who responded (defined as 40% improvement in Montgomery–Asberg Depression Rating Scale [MADRS] score) at 6 months. However, both interventions increased response rates compared with interpersonal psychotherapy alone (response rate: 707 people aged 18–74 years with dysthymia; 60% with sertraline alone *v* 58% with sertraline plus interpersonal psychotherapy *v* 47% with interpersonal psychotherapy alone; P = 0.02 for sertraline or sertraline plus interpersonal psychotherapy *v* interpersonal psychotherapy alone). [28] Similar results were found after a further 18 months' follow-up. [29] The study did not perform intention to treat analyses, analysis was based on treatment completers. The second subsequent RCT found no significant difference in the proportion of people achieving remission with short-term psychodynamic supportive psychotherapy alone compared with therapy plus antidepressant combined over 24 weeks (208 outpatients, 18–65 years old, with mild to moderate depression; 32% with psychotherapy *v* 42% with antidepressant plus psychotherapy; P = 0.143). [29] Subgroup analysis found that combination therapy was more effective in people with depression and comorbid personality disorders at 24 weeks (23/49 [47%] with combination therapy *v* 7/36 [19%] with pharmacotherapy alone; P < 0.01) compared with people without comorbid personality disorders at 24 weeks (8/23 [34%] with combination therapy *v* 6/20 [30%] with pharmacotherapy alone; P = 0.74). [30]

Older adults:
We found one RCT (102 people aged > 60 years with major depressive disorder) that compared three interventions: desipramine plus cognitive behavioural therapy (CBT), desipramine alone, and CBT alone. [31] It found that all three groups showed a significant reduction in symptoms from baseline as assessed using the Hamilton Depression Rating Scale (HAM-D) after 16–20 weeks of treatment (change in HAM-D score: –0.20 with desipramine alone *v* –0.36 with CBT alone *v* –0.41 with desipramine plus CBT; P < 0.05 for all comparisons). It found that combination treatment significantly improved symptoms over 16–20 weeks compared with desipramine alone (P < 0.05). It found no significant difference between combination treatment and CBT alone (reported as not significant, CI not reported). It found no significant difference among groups in the proportion of people who withdrew for any cause (34% with desipramine alone *v* 23% with CBT alone *v* 33% with desipramine plus CBT therapy; P = 0.52).

Harms: The systematic reviews [26] [27] and one subsequent RCT [28] gave no information on adverse effects. One RCT found no significant difference in somatic complaints or adverse events between combination therapy and pharmacotherapy alone. [29]

Comment: **Clinical guide:**
The evidence suggests that a combination of antidepressants and psychotherapy is better than either alone. In practice, however, choices will be limited by patient preferences and by the availability of different psychotherapies. The emerging consensus seems to be that medication could be used for rapid symptom relief, and that psychotherapies are better at preventing relapse.

OPTION NON-DIRECTIVE COUNSELLING FOR INITIAL TREATMENT

Symptom severity
Compared with usual care/no treatment Brief non-directive counselling on symptoms of depression may be more effective at reducing symptoms in the short term (less than 6 months) in adults with recent onset psychological problems including depression (low-quality evidence).

For GRADE evaluation of interventions for depression in adults: psychological treatments and care pathways, see table, p 20 .

Benefits: We found one systematic review [32] and one subsequent RCT, [33] which examined the effects of non-directive counselling on symptoms of depression. The review found that brief, non-directive counselling may improve symptoms over 6 months, although the improvement may not be maintained in the longer term (see table 1, p 17). [32] RCTs found insufficient evidence to assess the relative efficacy of drug and non-drug treatment in severe depression (see comment below). The subsequent RCT found that counselling (8 sessions) significantly reduced anxiety and depression compared with no treatment after 8 weeks (366 women, aged 18–50 years with symptoms of anxiety and depression; difference in depression scores from baseline: results presented graphically; P = 0.001 for counselling *v* no treatment). [33]

In older adults:
We found no RCTs specifically in older adults.

Harms: The systematic review [32] and the RCT [33] gave no information on adverse effects.

Comment: See comment on cognitive therapy, p 9 .

OPTION BEFRIENDING FOR INITIAL TREATMENT

Treatment success
Compared with waiting list control Befriending may be more effective at increasing the proportion of women with remission of symptoms at 13 months in women with mild chronic depression (low-quality evidence).

For GRADE evaluation of interventions for depression in adults: psychological treatments and care pathways, see table, p 20 .

Benefits: We found one small RCT (86 women with chronic depression, aged > 18 years, primarily aged 25–40 years), which compared befriending versus waiting list control. [34] Initial identification was by postal screening of women registered with, but not attending, primary care and probably with only mild depression. The RCT found that befriending significantly increased the proportion of women with remission of symptoms at 13 months compared with waiting list control (proportion of women in remission: 65% with befriending *v* 39% with control; P < 0.05; NNT 4, 95% CI 2 to 18).

Older adults:
We found no systematic review or RCTs specifically in older adults.

Harms: The RCT gave no information on adverse effects. [34]

Comment: In the RCT, 14% of women in the befriending group and 12% of women in the waiting list control group were taking antidepressant drugs. [34] Fewer than half the women screened by post were interested in befriending as a treatment option.

Clinical guide:
Befriending is an attempt to address lack of support and poor social networks in people who are depressed. Although this is an interesting approach, there is not enough evidence to support befriending as a routine treatment for depression.

OPTION PROBLEM-SOLVING THERAPY FOR INITIAL TREATMENT

Treatment success
Compared with placebo/control We don't know whether problem solving is more effective at treating people with mild depression or dysthmia (very low-quality evidence).

Compared with placebo (in older adults) Problem-solving treatment-primary care seems to be no more effective at increasing remission rates in older people with dysthymia and minor depression (moderate-quality evidence).

Symptom severity
Problem-solving therapy provided by community mental health nurses compared with usual care from a GP We don't know whether problem-solving provided by community mental health nurses is more effective at improving symptoms in people with depression (very low-quality evidence).

Compared with placebo (in older adults) Problem-solving treatment-primary care is no more effective at improving symptoms (measured as a decrease in Hopkins Symptom Checklist Depression Subscale [HSCL-D]-20 score) at 11 weeks in older people with dysthymia and minor depression (high-quality evidence).

For GRADE evaluation of interventions for depression in adults: psychological treatments and care pathways, see table, p 20 .

Benefits: We found one systematic review of psychological therapies in primary care, including problem-solving therapy, [15] two subsequent RCTs, [35] [36] and one additional RCT. [37] The systematic review (search date not reported, 4 RCTs of problem-solving therapy) did not provide a specific analysis of problem-solving therapy in moderate depression but found no significant difference between problem-solving therapy and placebo in people with mild depression or dysthymia (see table 1, p 17). The first subsequent RCT (452 people with a range of depressive disorders, including adjustment disorders and dysthymia) recruited people from a community survey in nine European rural and urban centres. People received problem-solving therapy (128 people), a group course on depression prevention (108 people), and a control treatment (treatment not specified; 189 people). The RCT found a significant decrease in the proportion of people who were depressed 6 months after receiving problem-solving treatment compared with people who had received a control treatment (see table 1, p 17). [35] However, there was no significant difference between problem solving and control treatment in rates of depression at 1 year after treatment. The second subsequent RCT (247 people) found no significant differences in a range of outcomes after 8 or 26 weeks of treatment between problem-solving treatment provided by community mental health nurses compared with usual care from a general practitioner (P > 0.05). [36] A subanalysis of people with moderate or severe depression (77 people) on the revised clinical interview schedule found a borderline significant improvement in symptoms of depression after 8 weeks of problem-solving treatment provided by community mental health nurses compared with usual care from a general practitioner. However, this difference was not significant at 26 weeks. The additional RCT (70 people) found no significant difference in outcomes at 8 or 26 weeks between problem-solving therapy by community nurses and usual general practitioner care (see table 1, p 17). [37] RCTs found insufficient evidence to assess the relative efficacy of drug and non-drug treatment in severe depression (see comment below).

In older adults:
We found one RCT (415 people with minor depression or dysthymia, mean age 71 years), which compared three treatments; problem-solving treatment–primary care (PST-PC; 6 treatment sessions over 10 weeks), paroxetine (10–40 mg/day), and placebo. [38] The RCT found no significant difference between PST-PC and placebo in improvement in depressive symptoms (measured as a decrease in Hopkins Symptom Checklist Depression Subscale [HSCL-D]-20 score) after 11 weeks (mean decrease in HSCl-D-20 score: 0.52 with PST-PC *v* 0.40 with placebo; P = 0.13). However,

the improvement in depressive symptoms was significantly more rapid (weeks 2–11) in people receiving PST-PC compared with those receiving placebo (P = 0.01). It found similar rates of remission (defined as HDRS < 7) for dysthymia and minor depression for both treatment groups (dysthymia: 32/63 [51%] with problem-solving therapy *v* 25/62 [40%] with placebo; minor depression: 22/50 [44%] with problem-solving therapy *v* 28/57 [49%] with placebo; significance not assessed).

Harms: The review [15] and RCTs [35] [36] [37] [38] gave no information on adverse effects.

Comment: See comment on cognitive therapy, p 9 .

QUESTION **What are the effects of psychological interventions to reduce relapse rates in mild to moderate or severe depression?**

OPTION **COGNITIVE THERAPY TO PREVENT RELAPSE**

Relapse rates

Compared with antidepressants or usual clinical management Cognitive therapy may be more effective at reducing relapses at 1–2 years after stopping treatment (very low-quality evidence).

For GRADE evaluation of interventions for depression in adults: psychological treatments and care pathways, see table, p 20 .

Benefits:

Cognitive therapy versus antidepressant drugs or usual clinical management:

We found one systematic review [12] and five subsequent RCTs, [39] [40] [41] [42] [43] which compared cognitive therapy or various forms of usual clinical management versus antidepressant drugs in people with mainly mild to moderate depressive disorders. The review found limited evidence that cognitive therapy reduced relapse (Beck Depression Inventory [BDI] score > 16) compared with antidepressant drugs or antidepressant drugs plus cognitive therapy (search date not reported, 261 people, mean age 39.3 years; proportion who relapsed: 30% with cognitive therapy *v* 60% with antidepressant drugs or antidepressant drugs plus cognitive therapy). [12] The first subsequent RCT compared cognitive behavioural therapy versus usual care (antidepressant drugs) in people who had largely responded to antidepressant drugs but had some residual depressive symptoms. [39] It found that fewer people relapsed with continued CBT than with antidepressant drugs after 2 years (40 people; relapse: 25% with CBT *v* 80% with clinical management; P < 0.001). [39] A 6-year follow-up study of these people compared the effects of cognitive therapy versus clinical management (20 people randomly assigned to each treatment arm) after successful treatment with antidepressant drugs. It found that cognitive therapy significantly decreased the rate of relapse after discontinuation of antidepressant drugs compared with clinical management (8/20 [40%] with cognitive therapy *v* 18/20 [90%] with clinical management; P = 0.001). [44] The second subsequent RCT compared maintenance cognitive behavioural analysis system of psychotherapy (CBASP) versus assessments only over 1 year. It found that CBASP significantly reduced relapse compared with assessment only (82 people with a depressive disorder who had responded to CBASP, mean age 45 years, 67% female; recurrence: 11% with CBASP *v* 32% with assessment only; P < 0.05). [40] The third subsequent RCT compared 8 weeks of mindfulness-based cognitive therapy (a manualised group skills training programme) with treatment as usual over 1 year. It found that in people with three or more previous episodes of depression, group cognitive therapy significantly reduced relapse compared with treatment as usual after 60 weeks (75 people in remission or recovered from depression, recruited through general practitioners or advertisements, mean age 45 years; proportion who relapsed: 36% with group cognitive therapy *v* 78% with treatment as usual; P < 0.002). [41] In people with two previous episodes of depression there was no evidence of benefit. The fourth subsequent RCT compared fluoxetine alone versus fluoxetine plus cognitive therapy. It found no difference in rates of relapse after 6 months (132 people with major depressive disorder, who had responded to fluoxetine; proportion who relapsed: about 7% in both groups). [42] The fifth subsequent RCT (104 people with moderate to severe depression) was a 12-month continuation study of people who had responded to either cognitive therapy or antidepressant medication. [43] People who had responded to drug treatment were randomised to continue medication or withdrawal onto pill placebo. The RCT found that people who had cognitive therapy were significantly less likely to experience a relapse compared with those withdrawn onto pill placebo (31% with cognitive therapy *v* 76% with pill placebo; P = 0.004; absolute numbers not reported). The RCT found no significant difference in relapse rates between cognitive therapy and continued antidepressant treatment (31% with cognitive therapy *v* 47% with antidepressant drugs; P = 0.20; absolute numbers not reported). [43]

Older adults:

We found no systematic review or RCTs specifically in older adults.

Harms: See harms of antidepressant drugs in review on depression in adults: drug and physical treatments.

Comment: The review did not present information on the proportion of people who recovered and continued to remain well after 2 years. [12] The largest RCT identified by the review found that only a fifth of people remained well over 18 months' follow-up, and that there were no significant differences between interpersonal psychotherapy, cognitive therapy, or drug treatment. [12] Further large-scale comparative studies of the long-term effectiveness of treatments in people with all severities of depressive disorders are needed.

OPTION RELAPSE PREVENTION PROGRAMME

Symptom severity
Compared with usual care Relapse prevention programmes (primary care visits, patient education, follow-up telephone calls) are more effective in improving depressive symptoms at 1 year in people with recurrent major depression or dysthymic disorders who have recovered after 8 weeks of antidepressant treatment (moderate-quality evidence).

Relapse rates
Compared with usual care Relapse prevention programmes (primary care visits, patient education, follow-up telephone calls) and usual care are equally effective at reducing relapse rates (high-quality evidence).

For GRADE evaluation of interventions for depression in adults: psychological treatments and care pathways, see table, p 20 .

Benefits: We found two systematic reviews which compared a relapse-prevention programme with usual care. [45] [46] The reviews found that relapse prevention (2 primary care visits, patient education, and 3 follow-up telephone calls) significantly improved depressive symptoms over 1 year compared with usual care (search dates 2002 and 2003, 1 RCT, 386 people aged > 18 years with recurrent major depression or dysthymic disorder, who had largely recovered after 8 weeks of antidepressant treatment; results presented graphically; P = 0.04). However, they found no significant difference in relapse rates over 1 year (35% with relapse prevention *v* 34.6% with usual care; P value = 0.20; [46] RR 0.95, 95% CI 0.55 to 1.62 [45]).

Older adults:
We found no systematic review or RCTs specifically in older adults.

Harms: The RCT included in the reviews gave no information on adverse effects. [47]

Comment: **Clinical guide:**
Although there is limited evidence to support the use of relapse-prevention programmes, clinicians may wish to consider introducing elements of the relapse-prevention programme as part of a broader care pathway for the management of depression.

QUESTION What are the effects of psychological interventions to improve delivery of treatments in mild to moderate or severe depression?

OPTION CARE PATHWAYS

Symptom severity
Compared with usual care Care pathways (such as collaborative working between primary care clinicians and psychiatrists, intensive patient education, disease management, case management, and telephone support) may be more effective at improving symptoms and response rates at 4–12 months (low-quality evidence).

Compared with usual care (in older adults) Care pathways (such as community mental health teams, community nurse management team, collaborative care, home-based programme of detecting and managing depression, physician care with treatment recommendations) are more effective at improving symptoms and at increasing the proportion of people who respond at 3–12 months (moderate-quality evidence).

Relapse rates
Recurrence prevention programmes compared with usual care or other treatments Recurrence prevention programmes alone or combined with cognitive therapy, or psychiatric consultation and usual care seem to be equally effective at improving relapse rates at 6 months (moderate-quality evidence).

Treatment success
Compared with usual care It seems continuing case management delivered by nurses is more effective at increasing remission rates at 7–24 months (moderate-quality evidence).

Compared with usual care (in older adults) Program to Encourage Active, Rewarding Lives for Seniors (PEARLS) is more effective at increasing the proportion of people with minor depression or dysthymia achieve complete remission at 12 months (high-quality evidence).

Note

It is uncertain whether care pathways, delivered for several months only, improve the effectiveness of treatment for depression over longer periods of 2–5 years. not improve depressive symptoms compared with usual general practitioner care.

For GRADE evaluation of interventions for depression in adults: psychological treatments and care pathways, see table, p 20 .

Benefits:

We found four systematic reviews [45] [46] [48] [49] and 10 subsequent RCTs. [50] [51] [52] [53] [54] [55] [56] [57] [58] [59] The first review (search date 2003, 29 RCTs, total number of people not reported) compared educational and organisational depression-management interventions with usual care. [46] The second review (search date 2002, 6 RCTs, 8410 people) examined the effectiveness of disease-management programmes for diagnosis and treatment of depression. [48] The third systematic review (search date 2002, 10 RCTs, 4196 people) compared the effectiveness of disease-management programmes versus usual care for depression. [45] The fourth systematic review (search date 2003, 13 RCTs, 5784 people) examined the effectiveness of case management (defined as intervention for continuity of care including at least systematic symptom monitoring) in improving depression. [49] Most of the interventions in the RCTs included in the reviews consisted of two or more components delivered in people with mild to moderate depression in primary care. [45] [46] [48] [49] Individual components of care pathways included: screening for depression; patient education; shared case management between primary care physician, psychiatrist, and psychologist (collaborative care); provision of written or audiovisual materials for people with depression; active follow-up; active response to results of follow-up; group psychoeducation; patient checklists; clinician education or care guidelines for clinicians; use of patient-centred motivational approaches; and pharmacy feedback. The first two reviews did not perform a meta-analysis and, for these reviews, it was not possible to determine which individual component of the interventions were effective. [46] [48] However, the first review suggested that care pathways including elements of nurse-delivered case management, clinician education, and collaborative working improved outcomes compared with usual care. It also suggested that care guidelines for clinicians did not improve outcomes unless accompanied by interventions such as case management. [46] The fourth review conducted a subgroup analysis on the effectiveness of "complex" compared with "standard" care pathways in depression, where "complex" and "standard" were distinguished by the number and type of element in the care pathway. The review found similar effect sizes in depression outcomes for the standard and complex care pathways (standard care: 3 RCTs 869 people; SMD –0.40, 95% CI –0.64 to –0.17; complex care: 7 RCTs, 3093 people; SMD –0.38, 95% CI –0.64 to –0.11; significance of standard *v* complex care not assessed). [49] The second review included only RCTs that evaluated screening for depression in primary care as part of the care pathway. Five of six included RCTs found improved recovery from depression after intervention compared with usual care. [48] The third review found that, compared with usual care, disease-management programmes significantly reduced the severity of depression after 4–12 months (10 RCTs, 4196 people; RR 0.75, 95% CI 0.70 to 0.81). [45] The fourth review found that case management significantly reduced depressive symptoms after 6–12 months compared with usual care (11 RCTs, 4320 people; SMD –0.40, 95% CI –0.60 to –0.20). [49] We found two long-term follow-ups of RCTs of depression management programmes included in the reviews, [60] [61] and one RCT of long-term follow-up of an RCT of case management included in some of the reviews. [62] The first long-term follow-up found that a multifaceted quality-improvement programme (including clinician education, case management delivered by nurses, and patient education) significantly reduced prevalence of probable depressive disorder compared with usual care at 57 months (46 primary care practices, 1356 adults with depression; AR for probable depressive disorder: 37% with quality improvement programme *v* 44% with usual care; ARR 6.6%, 95% CI 0.4% to 12.8%). [60] The second long-term follow-up RCT (116 people with major depression) compared enhanced acute-phase treatment of depression (involving combinations of clinician education, patient education, symptom monitoring, psychiatric review and adherence monitoring, focused on the first 6 weeks, with intermittent planned telephone contact or adherence monitoring up to 7 months) with usual care. [61] Hopkins Symptom Checklist score was measured as the primary outcome (mean baseline HSCL score 46.6). The RCT found no significant difference between enhanced care and usual care in symptoms of depression after 19 months (mean Hopkins Symptom Checklist score after 19 months: 16.4 with collaborative care *v* 16.3 with usual care; P = 0.97). [61] The RCT of long-term case management compared continuing case management delivered by nurses between 7 months and 24 months after starting treatment for depression versus usual care. It found that intervention increased remission rates (12 US primary care practices, 211 adults with major depression; numbers in remission: 74% with continuing case management *v* 41% with usual care; ARR 33%, 95% CI 7% to 46%). [62] The first subsequent RCT compared a patient educational compliance programme (provision of participant education

and support to encourage compliance with drug treatment) versus therapeutic drug monitoring (sertraline dose optimisation by determination of plasma levels and continued discussion with participant) versus usual care. [50] The RCT found that the educational compliance programme significantly increased response rate (defined as reduction in Montgomery–Asberg Depression Rating Scale [MADRS] score 50% or greater from baseline) compared with usual care at 24 weeks, while therapeutic drug monitoring did not (1031 people with major depression, being treated with sertraline; response: 71% with education *v* 68% with drug monitoring *v* 61% with usual care; P = 0.01 for education *v* usual care; P = 0.14 for drug monitoring *v* usual care, see comment below). [50] The second subsequent RCT compared a collaborative-care programme (patient education, structured follow-up, pharmacotherapy for people with severe or persistent depression, and adherence monitoring) versus usual care. [51] The RCT found that collaborative care significantly increased response rate (Hamilton Depression Rating Scale [HAM-D] score < 8) compared with usual care over 6 months (240 women, aged 30–60 years, with major depressive disorder; response: 73/104 [70%] with collaborative care *v* 32/107 [30%] with usual care; OR 5.52, 95% CI 3.06 to 9.95; NNT 3, 95% CI 2 to 4). [51] The third subsequent RCT compared a quality-improvement programme (evidence-based guidelines, and case management by telephone, including clinician feedback and patient education) with usual care. [52] The RCT (405 people aged 18 years and over, starting or changing treatment for major depressive disorder or dysthymic disorder) found that the quality-improvement programme significantly increased response rate (defined as a reduction in Hopkins Symptom Checklist-20 by 50% or greater from baseline) at 6 months compared with usual care (106/177 [60%] with quality improvement programme *v* 68/146 [47%] with usual care; OR 1.7, 95% CI 1.1 to 2.7). [52] The fourth subsequent RCT compared a collaborative care model (emphasising the role of clinical pharmacists, who provided management of antidepressant treatment, patient education, and treatment follow-up by telephone and clinic appointment) versus usual care. [53] The RCT found no significant difference in remission rate (Brief Inventory for Depressive Symptoms score < 9) between intervention and control groups after 6 months (125 people with depression; remission rate: 30/54 [56%] with collaborative care *v* 14/24 [58%] with usual care; P = 0.36). The study may have lacked power to detect a clinically significant difference. [53] The fifth subsequent RCT compared 12 sessions of group CBT plus case management versus CBT alone over 6 months. [54] It reported results for Spanish and English speakers separately, having found a significant effect of language on outcome, but did not report combined results. It found that more Spanish-speaking people had improved symptoms at 4 and 6 months with case management plus CBT compared with CBT alone (mean Beck Depression Inventory [BDI] score at 6 months: 18 with CBT plus case management *v* 25 with CBT alone; reported as not significant, CI not reported). [54] The sixth subsequent RCT compared an intervention to deliver guideline-based depression care (including outreach, phone contact and up to 4 educational meetings with clinician, provision of childcare and transportation) plus either antidepressant drug, supervised by a nurse practitioner, or CBT delivered by a psychotherapist compared with referral to community mental health services. [55] The RCT found that both drug and psychotherapeutic intervention significantly reduced depressive symptoms compared with community care after 6 months. However, the RCT found no significant difference between the two treatments (267 women with depression, 94% ethnic minority, 92% on low income; mean HAM-D score at 6 months: 5.2, 95% CI 3.0 to 7.3 with antidepressant drug plus guideline based care *v* 7.2, 95% CI 5.0 to 9.3 with CBT plus guideline based care *v* 10.1, 95% CI 8.0 to 12.3 with community referral; P < 0.01 for antidepressant drug *v* community referral; P = 0.006 for CBT *v* community referral; P = 0.6 for antidepressant drug *v* CBT). [55] The seventh subsequent RCT compared either telephone care management (patient education, monitoring of symptoms and adverse effects of antidepressants, and telephone care co-ordination) plus telephone CBT (8 sessions of up to 40 minutes each) or telephone care management alone versus usual care. [56] The RCT found that telephone care management plus telephone CBT significantly improved depression outcome (50% reduction in Hopkins Symptom Checklist Depression Scale) compared with usual care (100/172 [58%] with telephone care management plus telephone CBT *v* 76/176 [43%] with usual care; P = 0.005). However, there was no significant difference between telephone care management alone (without telephone CBT) and usual care (94/184 [51%] with telephone care management *v* 76/176 [43%] with usual care; P = 0.13). [56] The eighth subsequent RCT (267 people meeting the *Statistical Manual of Mental Disorders IV* (DSM)-IV diagnosis of a major depressive disorder) compared a depression recurrence prevention programme (patient education and telephone monitoring) alone (112 people) versus three other treatments: depression recurrence prevention programme plus psychiatric consultation (39 people); depression recurrence prevention programme plus individual CBT (10–12 sessions of 1 hour duration; 44 people); and usual care (72 people). [57] The RCT found no significant difference between any of the treatments in improvement of depression outcomes or relapse rates after 6 months (percentage of people with neither recovery nor remission after 6 months: 23% with recurrence-prevention programme alone *v* 12% with recurrence-prevention programme plus psychiatric consultation *v* 20% with recurrence-prevention programme plus cognitive therapy *v* 20% with usual care; reported as not significant; P values not reported). [57] The ninth subsequent RCT compared case management by nurse specialists (including patient monitoring, treatment planning, and care co-ordination) versus notification of

physician regarding diagnosis. [58] The RCT found no significant difference in depression symptoms (measured by mean Beck Depression Inventory [BDI] score) with care management compared with notification of physician at 3 or 12 months (268 people with major depression, dysthymia, or partially-remitted major depression, screened in general medicine clinics; 3 month Beck Depression Inventory [BDI] score: 20 with intervention *v* 22 with control; P = 0.43; 12-month BDI score: 18 with intervention *v* 20 with control; P = 0.51). [58] The tenth subsequent RCT compared a comprehensive care pathways programme (evidence-based prescribing, systematic follow-up, enhanced patient and general practitioner education, self management support, and encouragement of active participation of general practitioner and patient in treatment process) versus systematic follow-up (evidence-based prescribing and systematic follow-up only). [59] The RCT found no significant difference in response rate at 6 months between the comprehensive care pathways programme and systematic follow-up (211 people aged 18 years and over with major depression; response at 6 months; 47/101 [47%] with comprehensive care programme *v* 51/110 [46%] with systematic follow-up; OR 1.0, 95% CI 0.6 to 1.7). [59]

Older adults:

Both systematic reviews included RCTs that examined the effects of care pathways in depressed older people. [46] [48] The first systematic review included three such RCTs, [63] [64] [65] two of which did not appear in the second review. We found one subsequent RCT. [66] The first RCT compared care by a community mental health team (CMHT) versus usual general practitioner care in depressed elderly people. Care by the CMHT involved the person being seen within 3 weeks, assessed, and a report of recommendations sent to their general practitioner. The RCT found that intervention by a CMHT did not significantly improve depressive symptoms (as measured on the Geriatric Depression Scale [GDS-15]) after 18 months (93 people aged > 75 years, baseline GDS-15 score 5 or greater; numbers improving GDS-15 score: 26% with CMHT *v* 39% with usual care; P = 0.08). [63] The second RCT compared community nurse management versus usual general practitioner care. Community nurse management involved a nurse seeing the person weekly and attempting to implement a multidisciplinary management plan. The RCT found that the intervention significantly reduced symptoms of depression (as measured by the short CARE scale) after 3 months (96 older people with depression, short CARE score 6 or greater; change in depression scores: 2.57 with intervention *v* 1.26 with control; P = 0.05). The RCT also found that more people in the intervention group recovered (defined as a short CARE score < 6) compared with the usual-care group, but this difference was not significant (47% with intervention *v* 33% with controls; reported as not significant). [64] The third RCT, which was also included in the second review, compared collaborative care versus usual care. [65] Collaborative care involved a depression care manager (nurse or psychologist) who offered education, assisted in preparing a treatment plan, and either managed the person's antidepressant regimen alongside their primary care physician or gave 6–8 sessions of problem-solving therapy for each person. Eighty per cent of people received antidepressants and 30% received problem-solving therapy. The RCT found that compared with usual care (including antidepressant drugs), the addition of collaborative care significantly increased the proportion of people who responded (defined as > 50% reduction in depressive symptoms on the Symptom Checklist-90 [SCL-90]) over 12 months (1801 people aged > 60 years with major depressive disorder; 398/889 [45%] with collaborative care *v* 167/870 [19%] with usual care; OR 3.45, 95% CI 2.71 to 4.38). [65] The second systematic review [48] included one RCT in older people. [67] The RCT compared physician care with treatment recommendations versus usual physician care. Treatment recommendations involved encouraging the physicians to establish a diagnosis of depression, educate their patients about their diagnosis, discontinue medications that can cause depressive symptoms, initiate antidepressant drugs when appropriate, and consider referral to a psychiatrist. There was no significant difference in HAM-D scores at 6 months. However, physicians of intervention patients were more likely to diagnose depression and prescribe antidepressant drugs (175 people aged 60 years and over with HAM-D 15 or greater; diagnosed depression: 32% with treatment recommendations *v* 12% with usual care; P < 0.01; prescribed antidepressants: 26% with treatment recommendations *v* 8% with usual care; P < 0.01). [67] The first subsequent RCT (138 people with minor depression or dysthymia, aged 60 years and over) compared a home-based programme of detecting and managing depression (Program to Encourage Active, Rewarding Lives for Seniors [PEARLS]) versus usual care. [66] PEARLS involved problem solving, engaging in social and physical activities, and potential recommendations to peoples' physicians about antidepressant drugs. Treatment response was defined as a reduction in Hopkins Symptom Checklist-20 by 50% or greater from baseline, and remission was defined as a Hopkins Symptom Checklist-20 of less than 0.5. The RCT found a significant increase in the proportion of people with improved symptoms and with complete remission of depression at 12 months with PEARLS compared with usual care (improved symptoms of depression: 29/72 [40%] with PEARLS *v* 9/66 [14%] with usual care; OR 5.21, 95% CI 2.01 to 13.49; complete remission; 24/72 [33%] with PEARLS *v* 7/66 [11%] with usual care; OR 4.96, 95% CI 1.79 to 13.72).

Harms:

The reviews [45] [46] [48] [49] and subsequent RCTs [50] [51] [52] [53] [54] [55] [56] [57] [58] [59] [66] gave no information about adverse effects.

Comment: Some RCTs included in the reviews and subsequent RCTs made a unit of analysis error, not correcting for clustering, and analysing data by individual symptom scores, rather than by practice (by which they randomised). [45] [46] [48] [49] [50] [59] Failure to account for clustering leads to overestimates of the effect of the intervention, and increases the probability of type I errors.

Clinical guide:
Care pathways include treatments such as collaborative working between primary care clinicians and psychiatrists, intensive patient education, case management, and telephone support. Although the effectiveness or otherwise of specific elements of care pathways in the treatment of depression is not known, clinicians should, when feasible, consider introducing elements of care pathways to the management of their patients with depression.

GLOSSARY

Active follow up involves intensive follow up to assess adherence to the prescribed treatment, whether symptoms are improving, and whether any adverse effects are tolerable. Brief depression scales such as the Patient Health Questionnaire-9 (PHQ-9) may be used, which include details of depression symptom scores, and early warning signs of depression. Asking about adherence to antidepressant medication is also important. Alternatively, follow up may be face to face, or by telephone.
Active response to results of follow up involves proactively adjusting the treatment plan if a person with depression is not improving, is not adhering to treatment, or is having intolerable adverse effects. These adjustments may include changing the medicine or its dose, adding another form of treatment, or obtaining a specialist psychiatric opinion.
Befriending involves a person who is not depressed meeting the person with depression to talk and socialise for at least 1 hour a week, acting as a friend.
Brief, non-directive counselling Helping people to express feelings and clarify thoughts and difficulties; therapists suggest alternative understandings and do not give direct advice but try to encourage people to solve their own problems.
Care pathway A care pathway is a multidisciplinary plan of anticipated care.
Case management involves assigning a care manager to each person with depression, who co-ordinates the package of augmented care. The care manager may be a medical staff member, a practice nurse, a clinical psychologist, or a graduate mental health worker.
Cognitive behavioural therapy Brief (6–20 sessions over 12–16 weeks) structured treatment, incorporating elements of cognitive therapy and behavioural therapy. Behavioural therapy is based on learning theory and concentrates on changing behaviour. It requires a highly trained therapist.
Cognitive therapy Brief (20 sessions over 12–16 weeks) structured treatment aimed at changing the dysfunctional beliefs and negative automatic thoughts that characterise depressive disorders. It requires a highly trained therapist.
Dysthymic disorder Characterised by at least 2 years of depressed mood for more days than not, accompanied by additional symptoms that do not reach the criteria for major depressive disorder.
Effect size This expresses the degree of overlap between the range of scores in the control and experimental groups. The effect size can be used to estimate the proportion of people in the control group who had a poorer outcome than the average person in the experimental group; a proportion of 50% or less indicates that the treatment has no effect.
Interpersonal psychotherapy Standardised form of individual brief psychotherapy (usually 12–16 weekly sessions) primarily intended for outpatients with unipolar depressive disorders without psychotic features. It focuses on improving the person's interpersonal functioning and identifying the problems associated with the onset of the depressive episode.
Major depressive disorder Characterised by one or more major depressive episodes (i.e. at least 2 weeks of depressed mood or loss of interest accompanied by at least 4 additional symptoms of depression).
Mild to moderate depression Characterised by depressive symptoms and some functional impairment.
Problem solving therapy Consists of three stages: (1) identifying the main problems for the person, (2) generating solutions, and (3) trying out the solutions. Potentially briefer and simpler than cognitive therapy and may be feasible in primary care.
Psychodynamic supportive psychotherapy Aims to facilitate change by detecting and resolving underlying psychological conflicts. The treatment aims to be less challenging by incorporating supportive elements.
Severe depression Characterised by agitation or psychomotor retardation in addition to depressive symptoms and functional impairment with marked somatic symptoms. Treatments are considered to have been assessed in severe depression if the RCT included inpatients.
Use of patient centred, motivational approaches involves encouraging people to actively participate in their own care. Booklets or videos may be made available for patients and carers, which deliver information about the illness, its prognosis, its treatment, and simple cognitive and behavioural self treatment approaches. One or more professionals may deliver group teaching sessions on depression and how to recover.
High-quality evidence Further research is very unlikely to change our confidence in the estimate of effect.
Low-quality evidence Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Moderate-quality evidence Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Very low-quality evidence Any estimate of effect is very uncertain.

SUBSTANTIVE CHANGES

Care pathways (in mild to moderate depression) Two systematic reviews [45] [49] and four RCTs [52] [57] [59] [66] added; categorisation unchanged (Likely to be beneficial) but benefits and harms data enhanced.

Cognitive therapy (in mild to moderate depression) Two systematic reviews [17] [18] and two RCTs [19] [21] added; categorisation unchanged (Beneficial) but benefits data enhanced.

Cognitive therapy to prevent relapse One RCT [43] and one follow-up study [44] added; categorisation unchanged (Unknown effectiveness) but benefits data enhanced.

Interpersonal psychotherapy (in mild to moderate depression) One systematic review added; [18] categorisation unchanged (Beneficial) but benefits data enhanced.

Problem-solving therapy (in mild to moderate depression) Two RCTs added, [36] [38] categorisation unchanged (Unknown effectiveness) but benefits data enhanced.

Relapse prevention programme One systematic review added; [45] categorisation unchanged (Unknown effectiveness) but benefits and harms data enhanced.

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TABLE 1 **Effects of specific psychological treatments for depressive disorders.** [12] [13] [14] [15] [16] [17] [18] [23] [25] [32] [33] [35] [36] [37]

Evidence	Benefits	Disadvantages
Cognitive therapy		
8 SRs of psychological therapies including CT [12] [13] [14] [15] [16] [17] [18] [23]		Requires extensive training. Limited availability. CT in primary care suggests limited acceptability and effectiveness to some people
1 SR (search date not reported, 48 RCTs of psychological therapies, 2765 people, mean age 39.3 years). RCTs mainly in outpatients in secondary care; therefore, probably with mild to moderate depression; people with psychotic or bipolar symptoms were excluded. 20 RCTs compared CT *v* placebo or waiting list control and 17 compared CT *v* antidepressant drugs [12]	79% of people receiving placebo were more symptomatic than the average person receiving CT (P < 0.0001). [12] 65% of people receiving CT were less symptomatic than the average person treated with antidepressants (P < 0.0001)	
1 SR (search date 2002, 6 RCTs, 2 included in the first SR, [12] 883 people with major depression without psychotic features, mean age 30–40 years, 3 RCTs in psychiatric outpatients, 3 RCTs in primary care) comparing 3 interventions: psychotherapy (mainly CT [2 RCTs] and IPT [3 RCTs]), and antidepressant drugs (TCAs or phenelzine), and control (pill placebo or antidepressant plus usual care or supportive therapy) for an average of 16 weeks [13]	Psychotherapy significantly increased proportion of people in remission over 10–34 weeks compared with control (46% with psychotherapy *v* 24% with control; P < 0.0001). Remission defined as score of 6 or 7 on HAM-D. About 50% of control group withdrew from treatment compared with 22% receiving psychotherapy. [13] No results reported for CT alone	
1 SR (search date 1999, 63 RCTs and controlled clinical trials, 23 RCTs included in the first [12] or second [13] reviews, of brief psychological therapies (up to a maximum of 20 sessions) in people aged 16–65 years with mild to moderate depression. 43 studies in university psychology departments, 13 in psychiatry outpatient clinics, and 7 in primary care. 13 RCTs (886 people) compared psychological therapies *v* usual care. 16 RCTs (1024 people) compared CT *v* IPT, brief psychodynamic therapy, or supportive therapy [14]	All psychological therapies significantly increased proportion of people who recovered compared with usual care (13 RCTs, 886 people: recovery defined as score < 10 on Beck Depression Inventory Score or < 10 on HAM-D: OR 3.0, 95% CI 2.4 to 4.0). [14] CT increased proportion of people who recovered compared with usual care (12 RCTs, 654 people; OR 3.42, 95% CI 1.98 to 5.93). CT better than combined group of IPT, brief psychodynamic therapy, or supportive therapy at producing recovery (17 RCTs: 262/491 [53%] with CT *v* 196/533 [37%] with IPT, brief psychodynamic therapy, or supportive therapy; OR 2.4, 95% CI 1.4 to 4.2), but there was no significant difference between CT and IPT alone (2 RCTs, 275 people; recovery: OR 1.08, 95% CI 0.7 to 1.7 [14]	
1 SR [15] of psychological therapies in people with mild to moderate depression in primary care (search date not reported, 10 RCTs, 2 of CT, 1 of CT plus non-directive counselling, 1 IPT, and 2 non-directive counselling, 2 included in the previous reviews [12] [13] [14])	All psychological therapies slightly but significantly better than usual care (5 RCTs, 623 people; SMD 0.31, 95% CI 0.12 to 0.50; no other statistical assessment reported). No significant difference between psychological therapies and antidepressants (7 RCTs, 882 people; SMD –0.08, 95% CI –0.21 to –0.05). No results reported for CT alone [15]	
1 SR (search date 1998, 6 RCTs) which compared psychodynamic psychotherapy and CBT [16]	No significant difference between psychodynamic psychotherapy and CBT in numbers achieving remission or improving after treatment (P > 0.05) [16]	
1 SR (search date 2002, 11 RCTs), which compared CT *v* wait list (or no treatment), pill placebo, or attention/psychological placebo [17]	The review found an effect size of 0.77 for CT and control treatment in improving symptoms of depression, but the result was not significant (95% CI 0.44 to 1.10) [17]	
1 SR (search date 2002, 13 RCTs), which compared CT *v* IPT [18]	CT was significantly less effective compared with IPT in improving symptoms of depression (3 RCTs, 204 people; WMD for IPT *v* CT –2.16, 95% CI –4.16 to –0.15). [18] However, there was no significant difference in remission rates for the two treatments (56% with IPT *v* 47% with CT; RR 0.82, 95% CI 0.63 to 1.07)	

	Evidence	Benefits	Disadvantages
	One subsequent RCT (240 people aged 18–70 years with a DSM-IV diagnosis of major depressive disorder and a Hamilton Depression Score > 20) compared CT (60 people) *v* paroxetine (120 people) and pill placebo (60 people). [19] The RCT defined a response as a HAM-D of 12 or lower	The RCT found that both CT and paroxetine significantly improved symptoms of depression compared with pill placebo after 8 weeks (response rate: 43% with CT *v* 25% with pill placebo; P = 0.04; response rate: 50% with paroxetine *v* 25% with pill placebo; absolute numbers not reported; P = 0.001). However, the RCT found no significant difference in response rate between CT and paroxetine (P = 0.40). After 16 weeks, 58% of people in both the CT and paroxetine groups met the response criteria. The RCT found no significant difference in response rate between the 2 treatments (P = 0.92) [19]	
	1 SR (search date 1995, 4 RCTs in people aged > 55 years) which compared CT or behavioural therapy *v* no treatment [23]	CT and behavioural therapies significantly improved depressive symptoms *v* no treatment (mean difference in HAM-D –7.3, 95% CI –10.1 to –4.4 [23]	
Interpersonal psychotherapy			
	5 SRs [13] [14] [15] [18] [23] and 1 subsequent RCT [25] of psychological therapies including IPT	Two SRs did not report outcomes for IPT alone. [13] [15] 1 SR found that IPT increased the proportion of people who recovered compared with usual care (1 RCT, 185 people; OR 3.45, 95% CI 1.91 to 6.51). [14] The subsequent RCT found that IPT reduced numbers with depression (7% with IPT *v* 55% with no treatment; reported as significant). [25] 1 SR (search date 2002, 13 RCTs, 2199 people) found that IPT significantly improved symptoms of depression compared with placebo (9 RCTs, 653 people; WMD –3.57; 95% CI –5.98 to –1.16). [18] IPT significantly improved symptoms of depression compared with cognitive behavioural therapy (3 RCTs, 204 people; WMD –2.16, 95% CI –4.16 to –0.15). [18] However, there was no significant difference in remission rates for the two treatments (56% with IPT *v* 47% with CBT; RR 0.82, 95% CI 0.63 to 1.07). There were no significant differences between IPT, with or without antidepressant drugs, and antidepressant drugs alone in remission rates in the acute treatment of depression after treatment of 6 months or more (IPT alone *v* antidepressant drugs alone; RR 1.1, 95% CI 0.83 to 1.49; IPT plus antidepressant drugs *v* antidepressant drugs alone; RR 0.78, 95% CI 0.30 to 2.04). 1 SR in older people with depression found no significant difference between IPT or psychodynamic psychotherapy and no treatment (no further details reported) [23]	
Non-directive counselling			
	1 SR (search date not reported, 7 RCTs, people 18 years and over with recent onset psychological problems, including depression, in UK primary care) compared counselling *v* standard physician care, [32] and one subsequent RCT (366 women) [33]	Counselling *v* standard care significantly improved symptoms at 1–6 months (6 RCTs, 741 people; SMD –0.28, 95% CI –0.43 to –0.13), but no significant difference in the long term (4 RCTs, 447 people, > 6 months; SMD –0.07, 95% CI –0.26 to +0.12). [32] Over 1–6 months, 36% of people receiving counselling showed reliable and clinically important change compared with 23% receiving usual care. The subsequent RCT found that counselling improved symptoms of depression compared with no treatment (results presented graphically; P = 0.001) [33]	
problem-solving therapy			
	1 SR (search date not reported, 4 RCTs of PS therapy). [15] 2 subsequesnt RCTs [35] [36] and 1 additional RCT. [37]	No analysis of PS therapy alone in people with moderate depression. [15] See CT above. No significant difference between PS therapy and placebo pill in people with mild depression or dysthymia (2 RCTs, 439 people; reported as not significant, CI not reported) [15]	Requires some training. Limited availability

	Evidence	Benefits	Disadvantages
	One subsequent RCT (452 people aged 18–65 years with mild to moderate depression or adjustment disorders derived from a general population sample following a survey, probably with mild to moderate depression) compared PS, group treatment, and control. [35]	It found that PS significantly increased the proportion of people not depressed at 6 months, but no significant difference at 1 year. [35] (One subsequent RCT [247 people with a new episode of anxiety, depression, or reaction to life difficulties] compared PS treatment provided by community mental health nurses or usual care from community mental health nurses *v* usual care from a GP. [36]) The RCT found no significant differences in a range of outcomes after 8 or 26 weeks of treatment between PS treatment provided by community mental health nurses *v* usual care from a GP ($P > 0.05$). A subanalysis compared only those people with moderate or severe depression (77 people) on the revised clinical interview schedule. Reduction in CIS-R score was the clinical outcome. The RCT found a borderline significant improvement in symptoms of depression after 8 weeks of PS treatment provided by community mental health nurses compared with usual care from a GP (mean reduction in CIS-R score –8; 95% CI –15.67 to +0.34; $P = 0.041$). However, this difference was not significant at 26 weeks (mean reduction in CIS-R score +4.1; 95% CI –4.74 to +12.95; $P > 0.05$; no other data reported). [36] [One additional RCT (70 people aged 18–65 years in primary care with emotional disorders of at least 1 month) compared PS with usual care from GP. [37]] No significant difference between PS and usual care in symptoms at 8 or 26 weeks (mean CIS score at 8 weeks: 12.4 with PS *v* 10.5 with usual care; at 26 weeks: 9.3 with PS *v* 7.2 with usual care; reported as not significant, CI not reported) [37]	

CIS-R, Clinical Interview Schedule; CT, cognitive therapy; DSM-IV, *Diagnostic and Statistical Manual of Mental Disorders IV*; GP, general practitioner; HAM-D, Hamilton Depression Rating Scale; IPT, interpersonal psychotherapy; PS, problem solving; SR, systematic review; TCA, tricyclic antidepressant.

TABLE **GRADE evaluation of interventions for depression in adults: psychological treatments and care pathways**

Important outcomes	**Symptom severity, treatment success rates, relapse, social functioning, occupational functioning, quality of life, admission to hospital, self-harm, adverse effects**								
Number of studies (participants)	**Outcome**	**Comparison**	**Type of evidence**	**Quality**	**Consistency**	**Directness**	**Effect size**	**GRADE**	**Comment**
What are the effects of psychological treatments in mild to moderate or severe depression?									
49 RCTs (2885) [13]	Symptom severity	Cognitive therapy *v* placebo/ other treatments	4	–1	0	–1	0	Low	Quality point deducted for incomplete reporting of results. Directness point deducted for uncertainty about generalisability of results (different populations and different types of psychotherapies compared)
4 (?) [23]	Symptom severity	Cognitive/behavioural therapy *v* no treatment (in older adults)	4	0	0	–1	0	Moderate	Directness point deducted for uncertainty about generalisability of results
37 (3166) [13] [14] [15] [19]	Treatment success	Psychotherapies *v* control/usual care	4	–1	0	–1	0	Low	Quality point deducted for incomplete reporting of results. Directness point deducted for uncertainty about generalisability of results (different types and combinations of psychotherapies compared)
28 (2000) [16] [14] [18]	Treatment success	Cognitive therapy *v* other psychological treatments	4	–1	–1	–1	0	Very low	Quality point deducted for incomplete reporting of results. Consistency point deducted for conflicting results. Directness point deducted for uncertainty about generalisability of results (different populations and different types and combinations of psychotherapies compared)
2 (409)Ref = 14, 25 [14] [25]	Treatment success	Interpersonal psychotherapy for initial treatment *v* usual care/no treatment	4	–1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
12 (857) [18]	Symptom severity	Interpersonal psychotherapy for initial treatment *v* placebo/cognitive behavioural therapy	4	0	0	0	0	High	
At least 3 RCTs (at least 204 people) [18]	Treatment success	Interpersonal psychotherapy *v* cognitive behaviour therapy/antidepressants	4	–1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
3 (?) [23]	Treatment success	Interpersonal psychotherapy *v* no treatment (in older adults)	4	–2	0	–1	0	Very low	Quality points deducted for incomplete reporting of data. Directness point deducted for unclear measurement of outcomes
16 RCTs and 17 studies (at least 1842 people) [26] [28] [29] [27]	Symptom severity	Combination of psychological treatments and antidepressant drugs *v* either treatment alone	4	–1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
2 (915)[[29] [30] [28]	Treatment success	Combination of psychological treatments and antidepressant drugs *v* either treatment alone	4	–1	0	0	0	Moderate	Quality point deducted for no intention to treat analysis
1 (102) [31]	Symptom severity	Combining psychological treatments and antidepressant drugs for initial treatment *v* treatments alone (in older adults)	4	–2	0	0	0	Low	Quality points deducted for sparse data and incomplete reporting of results

Important outcomes	Symptom severity, treatment success rates, relapse, social functioning, occupational functioning, quality of life, admission to hospital, self-harm, adverse effects								
Number of studies (participants)	**Outcome**	**Comparison**	**Type of evidence**	**Quality**	**Consistency**	**Directness**	**Effect size**	**GRADE**	**Comment**
11 (1554) [32] [33]	Symptom severity	Non-directive counselling for initial treatment *v* usual care/no treatment	4	–1	0	–1	0	Low	Quality point deducted for incomplete reporting of results. Directness point deducted for inclusion of other conditions
1 (86) [34]	Treatment success	Befriending *v* waiting list control	4	–1	0	–1	0	Low	Quality point deducted for sparse data. Directness point deducted for uncertainty about benefit
3 (891) [15] [35]	Treatment success	Problem-solving therapy *v* placebo/control	4	–1	–1	–1	0	Very low	Quality point deducted for incomplete reporting of results. Consistency point deducted for different results at different endpoints. Directness point deducted for unclear measurement of outcome
2 (317) [36] [37]	Symptom severity	Problem-solving therapy provided by community mental health nurses *v* usual care from a GP	4	–1	0	–2	0	Very low	Quality point deducted for incomplete reporting of results. Consistency point deducted for different results at different endpoints. Directness points deducted for unclear measurement of outcome and inclusion of other disorders
1 (415) [38]	Symptom severity	Problem-solving treatment *v* placebo (in older adults)	4	0	0	0	0	High	
1 (232) [38]	Treatment success	Problem-solving treatment *v* placebo (in older adults)	4	–1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
What are the effects of psychological interventions to reduce relapse rates in mild to moderate or severe depression?									
at least 5 RCTs (694) [12] [39] [40] [41] [42] [43]	Relapse rates	Cognitive therapy *v* antidepressant drugs or usual clinical management	4	–2	–1	0	0	Very low	Quality points deducted for incomplete reporting of results and no long term results. Consistency point deducted for conflicting results
1 (386) [45] [46]	Symptom severity	Relapse prevention programme *v* usual care	4	–1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
1 (386) [45] [46]	Relapse rates	Relapse prevention programme *v* usual care	4	0	0	0	0	High	
What are the effects of psychological interventions to improve delivery of treatments in mild to moderate or severe depression?									
24 (9399) [45] [49] [50] [51] [56] [57] [58]	Symptom severity	Care pathways *v* usual care	4	–1	0	–1	0	Low	Quality point deducted for analysis flaws. Directness point deducted for too many comparators
1 (267) [57]	Relapse rates	Recurrence prevention programmes *v* usual care/other interventions	4	–1	0	0	0	Moderate	Quality point deducted for incomplete reporting of results
5 (2383) [62] [53] [50] [51] [52]	Treatment success	Care pathways *v* usual care	4	0	0	–1	0	Moderate	Directness point deducted for too many comparators
5 (2261) [63] [64] [65] [66] [67]	Symptom severity	Care pathways *v* usual care (in older adults)	4	0	0	–1	0	Moderate	Directness point deducted for too many comparators
1 (138) [66]	Treatment success	Care pathways *v* usual care (in older adults)	4	–1	0	0	+1	High	Quality point deducted for sparse data. Effect size point added for odds ratio greater than 2

Important outcomes	Symptom severity, treatment success rates, relapse, social functioning, occupational functioning, quality of life, admission to hospital, self-harm, adverse effects								
Number of studies (participants)	Outcome	Comparison	Type of evidence	Quality	Consistency	Directness	Effect size	GRADE	Comment

Type of evidence: 4 = RCT; 2 = Observational; 1 = Non-analytical/expert opinion. Consistency: similarity of results across studies
Directness: generaliseability of population or outcomes
Effect size: based on relative risk or odds ratio